

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of:

IZHAR

Serial No.: 09/411,863

Filed: October 4, 1999

For: EXOGENIC ALLELISM

Examiner: Kubelik, A.

[illegible]

Group Art Unit: 1638

Attorney
Docket: 00/20907
(previously 1620/3)

Commissioner of Patents and Trademarks
Washington, D.C. 20231

DECLARATION OF DR. VERED YESODI UNDER 37 CFR 1.132

I am presently employed as CEO at FertiSeed Ltd. the assignee of the present invention. I received my Ph.D degree from the Hebrew University in Department of Genetics, following which I worked for several years as a post-doctoral fellow in the Medical School of the Tel Aviv University in Israel.

Since the beginning of my career, I have published 9 scientific articles in highly regarded journals and books, and have presented my achievements at many international scientific conferences.

I have read and understood the invention described in the instant application.

I have read the Official Action issued with respect to the above-identified application, and in particular the Examiner's rejections of claims 47,49-51 and 55-57 under 35 U.S.C. § 112 first paragraph.

The PowerPoint presentation enclosed herewith illustrates the method steps described and claimed in the instant application. Figures 1-6 of the PowerPoint presentation illustrate results of a research study we conducted according to the guidelines provided in the instant application. These Figures conclusively show that the methodology described and claimed in the instant

application can be utilized to generate a plant exhibiting exogenic allelism thereby proving that the rejections of claims 47,49-51 and 55-57 under 35 U.S.C. § 112 first paragraph are unfounded.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

May 5, 2002

Dr. Vered Yesodi
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C.E.O.
FertiSecds Ltd.

Enc.:
CV of Dr. Vered Yesodi

Dr Vered Yesodi

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CURRICULUM VITAE- Dr Vered Yesodi**Personal data**

Date of Birth: 1959
Place of Birth: Haifa, Israel
Marital status: Married + 3 children.
Home address: 54 Irusim street, Reut, Israel
Tel. 08-9261803, 051-942144
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Education

- 1996-1998 Post doctorate position. Tel-Aviv University, Medical School,
Department of Embryology.
Research subject: Construction of chimeric vectors including the PKC
gene domains and GFP gene (as a reporter gene) and insertion as DNA
or cDNA into rat embryos
Supervisor: Prof. R. Shalgi.
- 1990-1996 Ph.D. Hebrew University Department of Genetic,
Thesis: Isolation and characterization of the sequence of origin of the
urf-s sequence which is associated with CMS in Petunia
Supervisors: Dr. N. Firon and Prof. S. Izhar.
- 1984-1986 M.Sc. Tel-Aviv University, Faculty of Life Sciences.
Thesis: Application of oligonucleotides complementary to Avocado
Sunblotch Viroid and Tobacco Mosaic Virus for diagnosis, typing and
control.
Supervisor: Prof. M. Bar-Josef
- 1981-1984 B.Sc. Ben-Gurion University, Department of Biochemistry.

Academic and professional experience

- 2000-Present Position: Acting CEO and R&D Manager.
At Fertiseeds Ltd., Rehovot. A company focusing on Agro Biotech
domains.
R&D subjects: Universal Male Sterility and Male Fertility Restoration.
- 1998-2000 Position: Research Director.
At the In-Vitro Fertilization (IVF) Laboratory, Racine IVF Unit, Lis
Maternity Hospital, Tel-Aviv Medical Center.
Research subjects:
· Characterization and analysis of mitochondrial DNA mutations in
human oocytes.

Dr Vered Yesodi

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- Development of Preimplantation Diagnosis in single human blastomeres.
- Construction of cDNA libraries from different stages of human oocyte and embryo development.

1988-1990 Position: Research Assistant.
At the Department of Virology, Volcani Center for Agricultural Research, under the supervision of Dr. A. Rosner.
Research subject:
Transgenic plants (Tobacco and Potato) containing the coat protein of PVY virus.

1986-1988 Position: Food technologist.
At food industry "Rimon" Kibbutz Givaat-Brenner

Dr Vered Yesodi

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Publications

1. Bar-Joseph, M., Segev, D., Blickle, W., Yesodi, V., Franck, A. and Rosner, A. (1986) Application of synthetic DNA probes for the detection of viruses. pp 13-23 In: Development and Application in Virus Testing. Ed. R.A.C. Jones and L. Torrance, Association of Applied Biologists, U.K. 312pp.
2. Rosner, A. and Yesodi, V. (1990). The subcloning and expression of the potato virus coat protein gene in *Escherichia coli*. *Phytophylactica* 22, 431-434.
3. Soferman-Avshalom, O., Yesodi, V., Tabib, Y., Gidoni, D., Izhar, S. and Firon, N. (1993). Detection of an open reading frame related to the CMS-associated urf-s in fertile *Petunia* lines and species and in other fertile Solanaceae species. *Theor. Appl. Genet.* 86: 308-311.
4. Firon, N., Gidoni, D., Yesodi, V., Nachshoni, D., Tabib, Y., Soferman, O. and Izhar, S. (1992). Molecular Biology of CMS and male fertility restoration in *Petunia*. *Israel J. Botany* 41(2).
5. Yesodi, V., Izhar, S., Gidoni, D., Tabib, Y. and Firon, N. (1995). Involvement of two different urf-s related mitochondrial sequences in the molecular evolution of the CMS-specific S-Pcf locus in *Petunia*. *Mol. Gen. Genet.* 248:540-546.
6. Yesodi, V., Izhar, S., Hauschner, H., Tabib, Y. and Firon, N. (1997a). Homologous recombination involving *cox2* responsible for a mutation in the CMS-specific mitochondrial locus of *Petunia*. *Mol. Gen. Genet.* 255:10-114.
7. Yesodi, V., Hauschner, H., and Firon, N. (1997b). An intact F1ATPase α -subunit gene and a pseudogene are detected in both male fertile and CMS *Petunia* mitochondria, at a different genome organization. *Curr. Genet.* 32:348-357.
8. Raz T., Eliyahu E., Yesodi V., Shalgi R. (1998). Profile of protein kinase C isozymes and their possible role in mammalian egg activation. *FEBS Letters* 431: 415-418
9. Yesodi V., Yaron Y., Lessing J., Amit A., Ben-Yosef D. (2002). The Mitochondrial DNA Mutation (*mtDNA*³²⁸⁶) In Human Oocytes: Correlation with Age and IVF Outcome. *J. of Ass. Rep. and Gen.* 19(2):60-66.

Appendix A

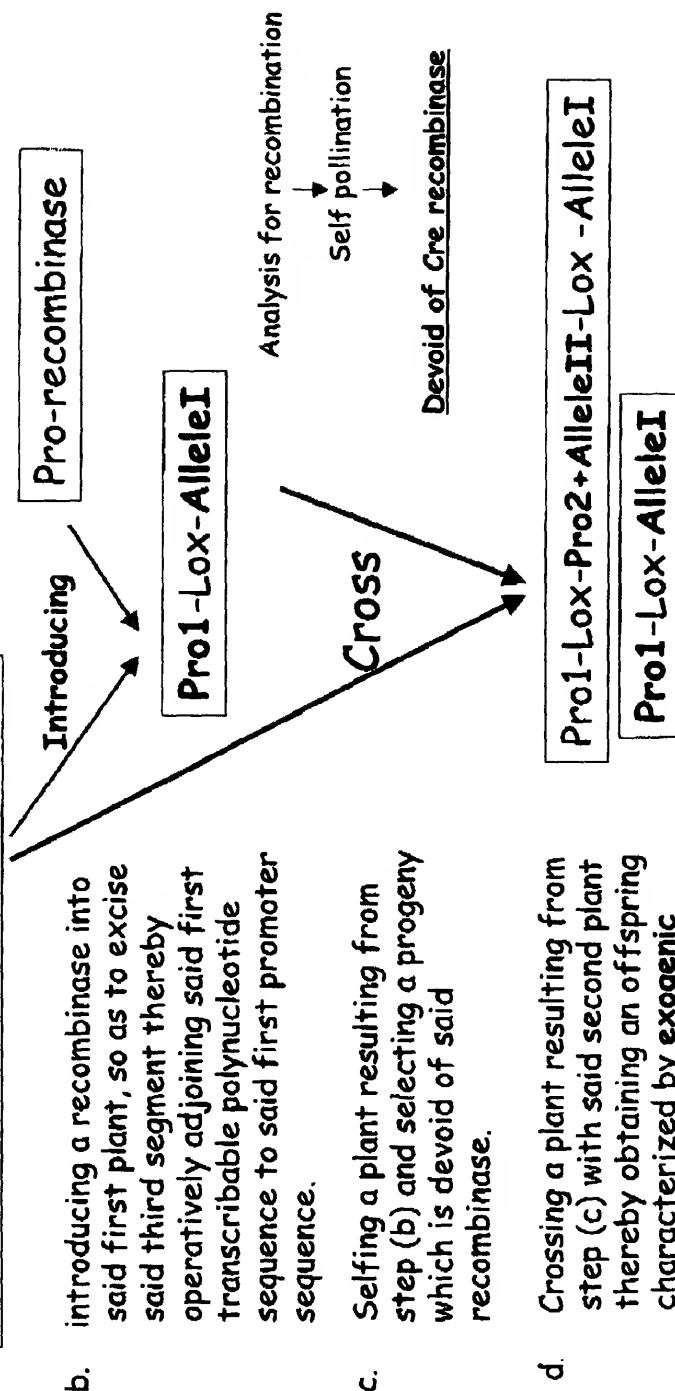


Illustration 1

Claim 47

- a. Providing a first and a second plant each including an expression cassette in the same chromosomal location

Pro1-Lox-Pro2+AlleleII- Lox - AlleleI



- b. introducing a recombinase into said first plant, so as to excise said third segment thereby operatively adjoining said first transcribable polynucleotide sequence to said first promoter sequence.
- c. Selfing a plant resulting from step (b) and selecting a progeny which is devoid of said recombinase.
- d. Crossing a plant resulting from step (c) with said second plant thereby obtaining an offspring characterized by exogenic allelism.



Claim 49

a. Providing a first and a second plant each including an expression cassette in the same chromosomal location

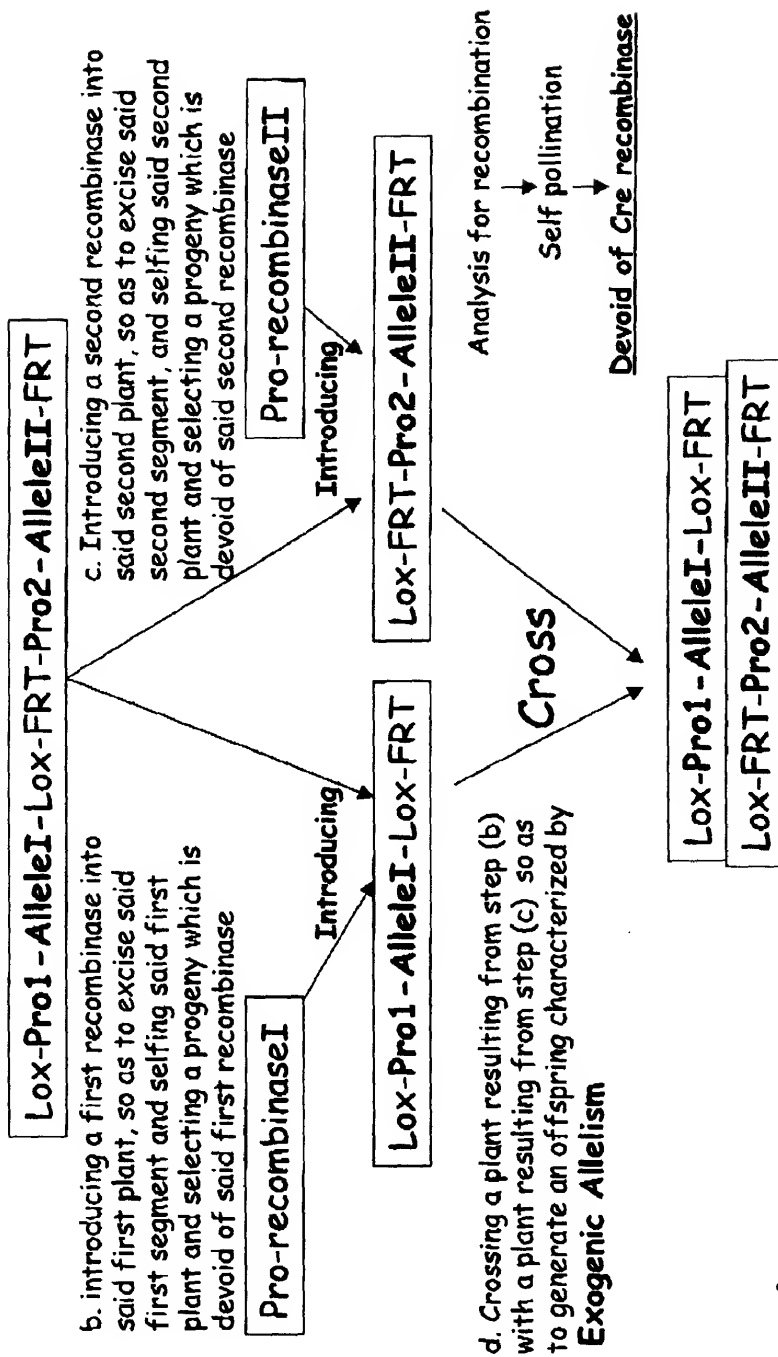
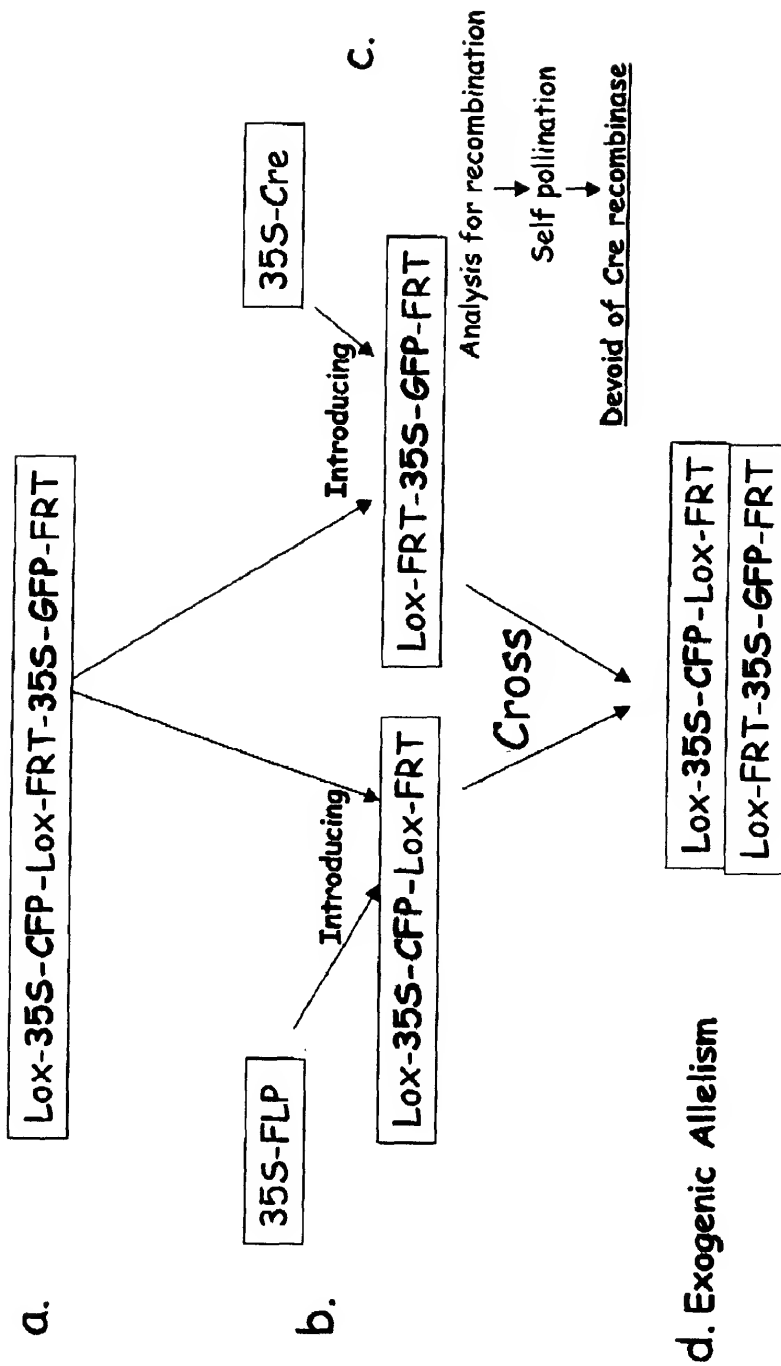


Illustration 3

A model for Claim 49

Using CFP as Allele I, GFP as Allele II and 35S as Promoters



**Figure 1****Claim49a**

"Providing a first plant and a second plant each including an expression cassette in the same chromosomal location"

Expression cassette construct

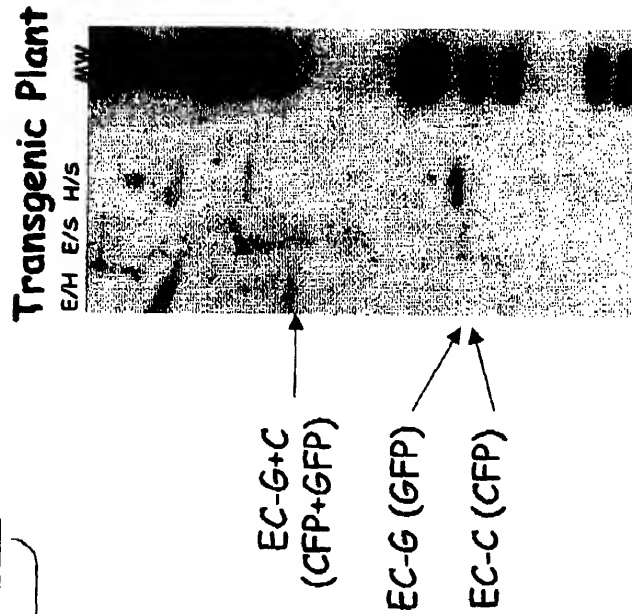
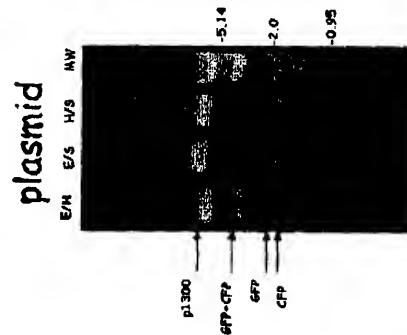
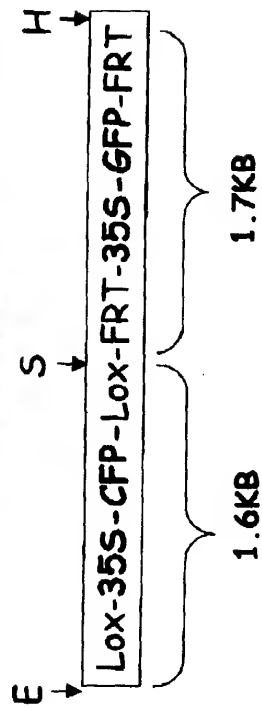




Figure 2

Claim49a (continued)

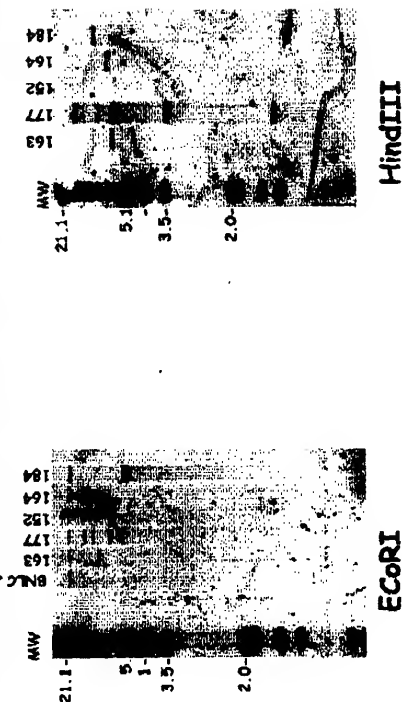
"Providing a first plant and a second plant each including an expression cassette in the same chromosomal location"

Phenotypic analysis of transgenic plant



Expression of the CFP and GFP in transgenic *Arabidopsis*

Copy number of Expression Cassette in transformed *Arabidopsis* plants





claim 47b and 49b and c

"introducing a recombinase"

Several methods can be used to introduce recombinase into plants which carry the Expression Cassette genes (EC-G+C). Among them we used the two following methods:

1. Sexual crosses between transformed plants, one carrying the Expression Cassette (EC-G+C) and one carrying an active recombinase (Cre+ or FLP+)

Plants expressing Cre recombinase



2. Transformation of plants which carry the Expression Cassette (EC-C+G) with DNA that carry expressible recombinase (Cre+ or FLP+) gene

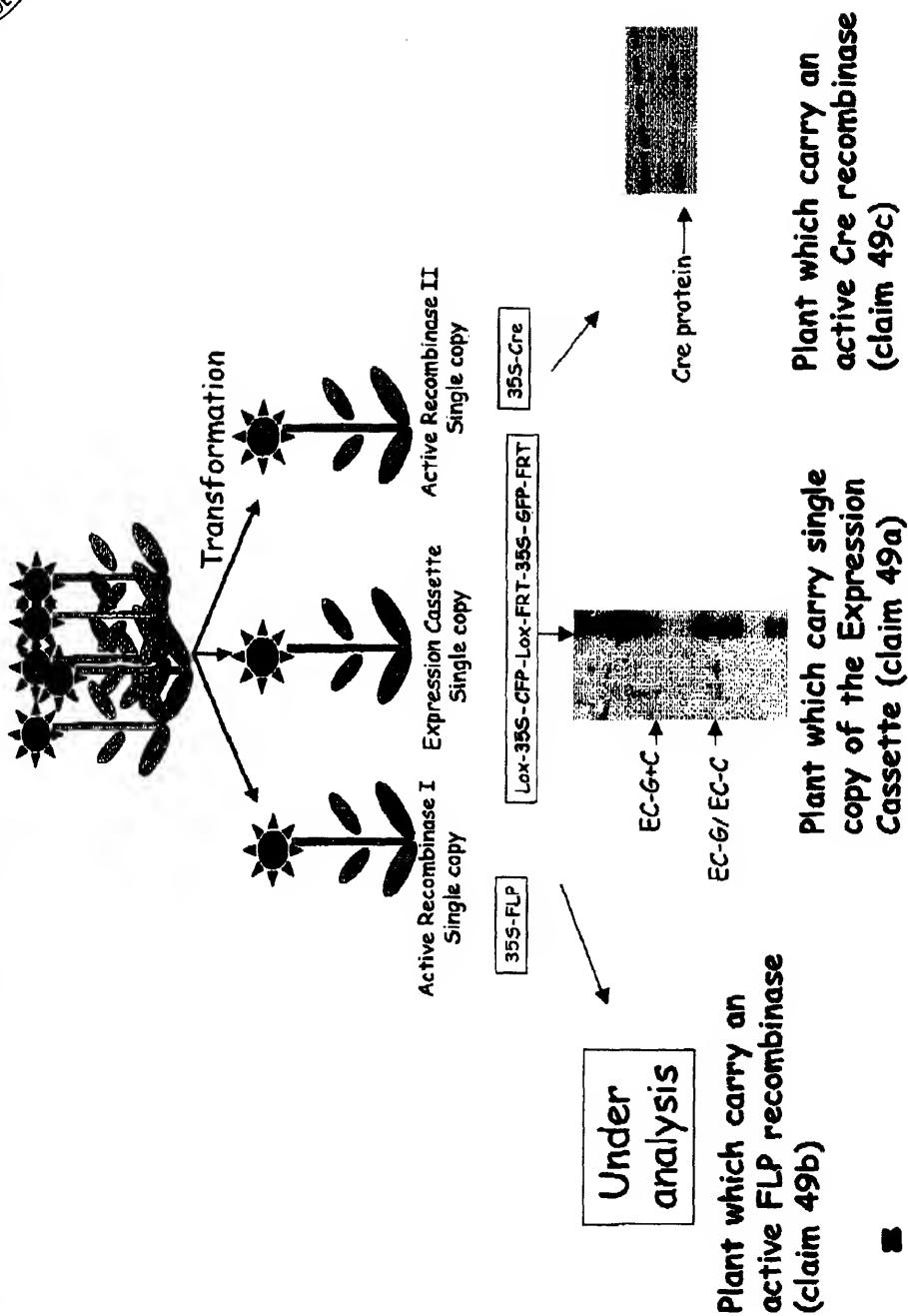
Illustration 4Claim 49a, b and c - summary

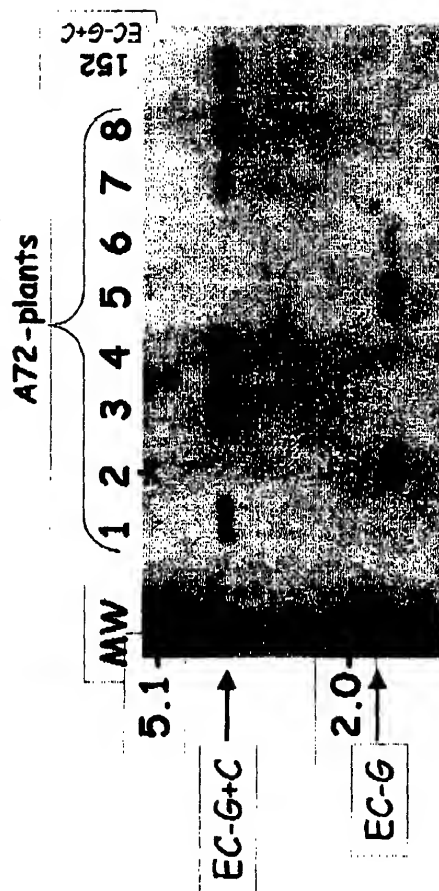


Figure 3

claim 49c and 47b

"Introducing a recombinase (first method)....so as to excise said first/third segment"

DNA analysis of plants resulting from cross between EC-G+C and Cre⁺ plants (T1)



Plants that showed excision (EC-G) received the active Cre-recombinase gene. Plants that contained both alleles (EC-G+C) did not receive the Cre-recombinase gene (data not show)



Figure 4

Claim 47c, 49c

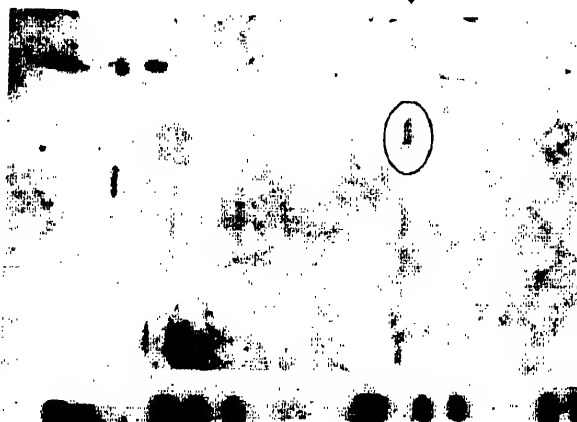
"and selfing said first plant and selecting a progeny which is devoid of said recombinase"

DNA analysis of plants following self pollination (T2) (cross A72-2)

A72-2-

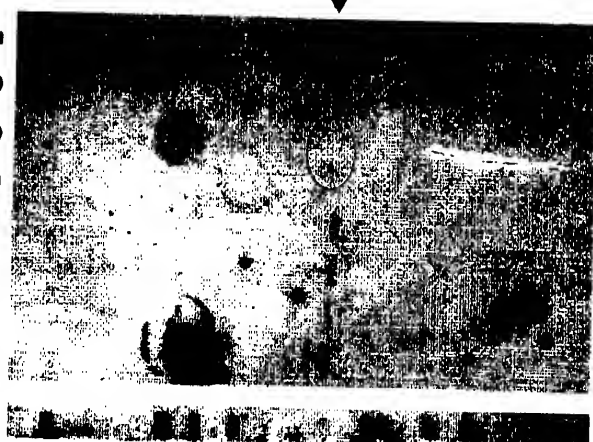
A72-2-

11 1098 6 5 3 1



A72-2-5 = Only
GFP (EC-6),
devoid of Cre
recombinase

Cre



*A72-2-5: excision event and devoid of Cre recombinase

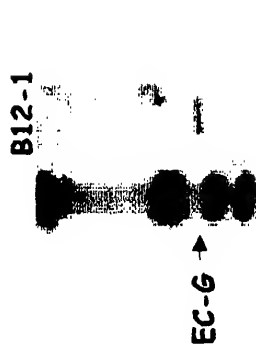


Figure 5

claim 47b, 49c

"introducing a recombinase " (second method)

Transformation of plants which carry the
Expression Cassette (EC-C+G) with DNA that
carry expressible Cre recombinase



"Selfing a plant resulting from step (c) and selecting a
progeny which is devoid of said recombinase"

DNA analysis of plants following self pollination (T2)

B12-1-5 = Only
GFP (EC-G),
devoid of Cre
recombinase

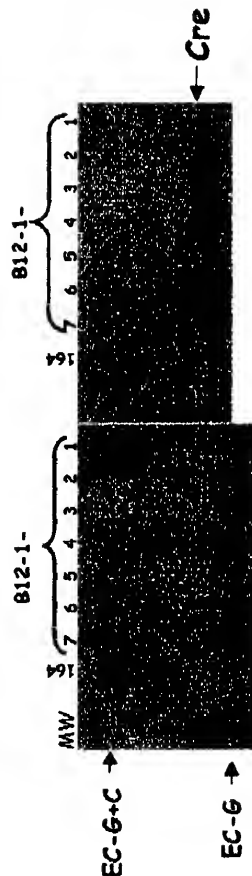
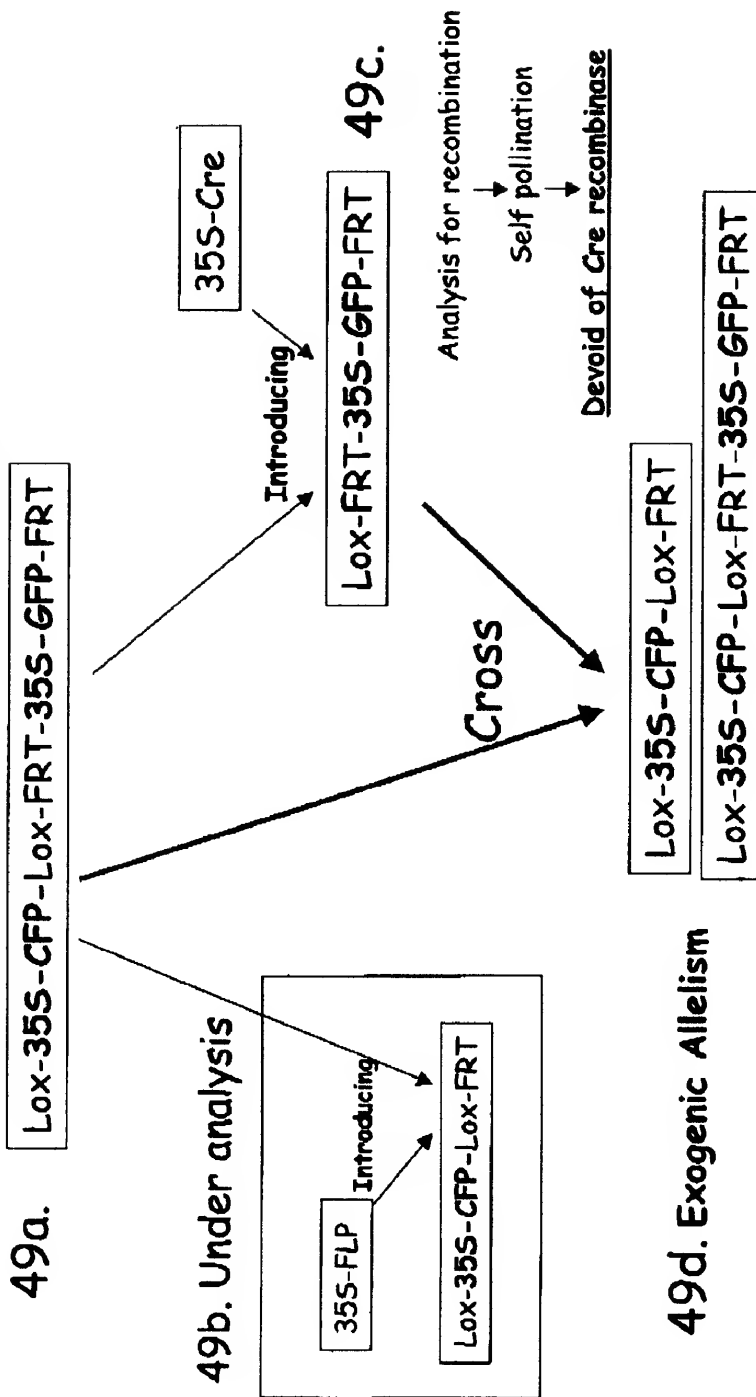




Illustration 5

A modified model for Exogenic Allelism using plant 49a and plant 49c as the two exogenes

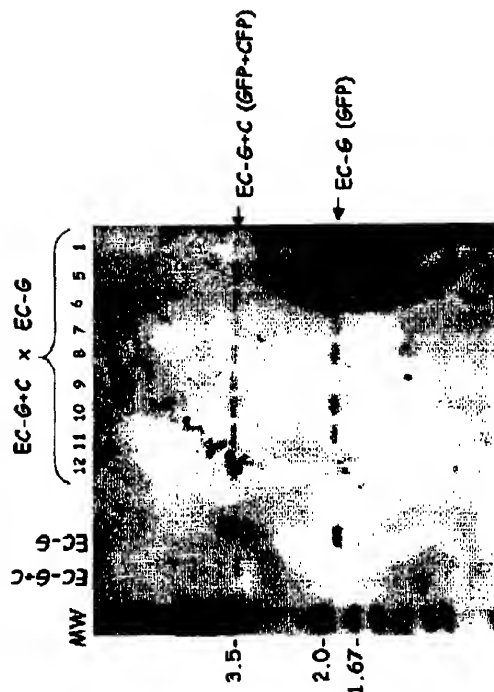


49d. Exogenic Allelism

**Figure 6****Claim 49d**

"Crossing a plant so as to generate an offspring characterized by
Exogenic Allelism"

DNA analysis of transgenic plants following cross between plant which
 carries EC-6+C DNA (as allele I) and plant which carries EC-6 DNA
 (as Allele II) at the same cromosomal location



**This results demonstrate plants which carry stable
 exogenes in an Exogenic Allelism position**